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# GUEST EDITORIAL

## Non-Metastasizing Melanoma?

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Halstead said in 1908, ''it is now as it was then and as it may ever be, concepts from the past blind us to facts that slap us in the face'' [1]. The last quarter century of cancer research has confronted surgeons with an increasingly complex picture of the biology of cancer, as well as major paradigm shifts in the rationales for surgical excisions of various cancers. Surgery has been and will continue to be the application of a mechanical therapy at one or more points in time to a disease whose biological lifespan is usually measured in decades. Surgery will also continue to be the most effective single modality for treating cancer into the foreseeable future. The success of surgery has, in part, created a dogma among surgeons that the pathway from malignant transformation to metastasis to vital organs might be long, but it is essentially irreversible and inevitable without successful (surgical) treatment.

This dogma is widely held, despite the lessons learned from Papanicolau screening for cervical cancer over more than a quarter of a century, and from basal cell carcinoma of the skin, which has been literally slapping us in the face forever. The second commonest fatal cancer of women worldwide has a biology that is reversible in the stages that lead up to invasive carcinoma, and the commonest cancer of white populations living in sunny climes has virtually no capacity to metastasize.

Cancer is a genetic disease, and there are many genetic pathways to an invasive cancer; some of these may abort, and others may be dead ends. Our paradigm for cancer has been symptomatic invasive and ultimately metastatic disease, the tip of the iceberg, the winning clones that emerge as the victors in the race to potentially fatal cancer when a susceptible tissue is exposed to a carcinogen. The old dogma must now confront the new reality. Cancers are now being detected that may remain in situ indefinitely or perhaps if invasive, may never metastasize. Screening for breast cancer, prostate cancer, melanoma, and colorectal cancer is confronting surgeons with these realities, which have long been known to gynaecologists and dermatologists!

The incidence of melanoma has been increasing at a rate of 3–7% a year in most white populations worldwide since measurements began in the early 1960s [2]. In the last decade, however, in some white populations the increase in incidence has been much higher, 15–43% a year [3]. Furthermore, these large increases in incidence have occurred in countries where melanoma mortality has plateaued or, in the case of Australia, where it is beginning to fall [4]. Rising incidence and falling mortality rates for a cancer can be explained by advances in the time of diagnosis through screening and cure through surgery [3]. Advancement of the time of diagnosis, however, may not be the whole story in melanoma.

In 1991 we reported on an analysis of a melanoma epidemic in the Hunter area Health Service of New South Wales, Australia [5]. The incidence of invasive melanoma in that area remained on a plateau of about 27/100,000 person years in the decade 1976–1986 for both males and females (Fig. 1). In the subsequent 2 years the incidence doubled to a peak of 55/100,000 person years in 1988 for males, and increased by 66% to a peak of 45/100,000 person years in females.

Similar rises were observed, particularly in men, in all states of Australia, and in New Zealand and Scotland [3]. In Australia these rises were attributed by some to advancement of the time of diagnosis consequent upon a national television program, ''Goodbye Sunshine,'' which was shown in late 1987 and early 1988 [6]. Both screenings of this tragic story of a young man with metastatic melanoma were followed by sudden increases in the diagnosis of cases of melanoma [6]. However, the sharp increases in the incidence of melanoma in some Australian male populations began prior to 1987 (Fig. 2), and this television program was not shown in either New Zealand or Scotland.

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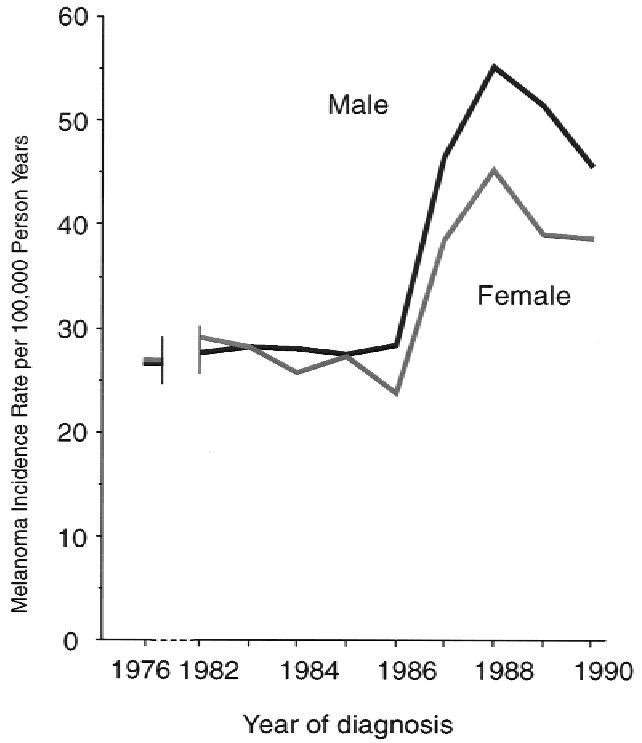


Fig. 1. Age-standardized incidence of melanoma in residents of the Hunter area Health Service of New South Wales, Australia, 1976–1990.

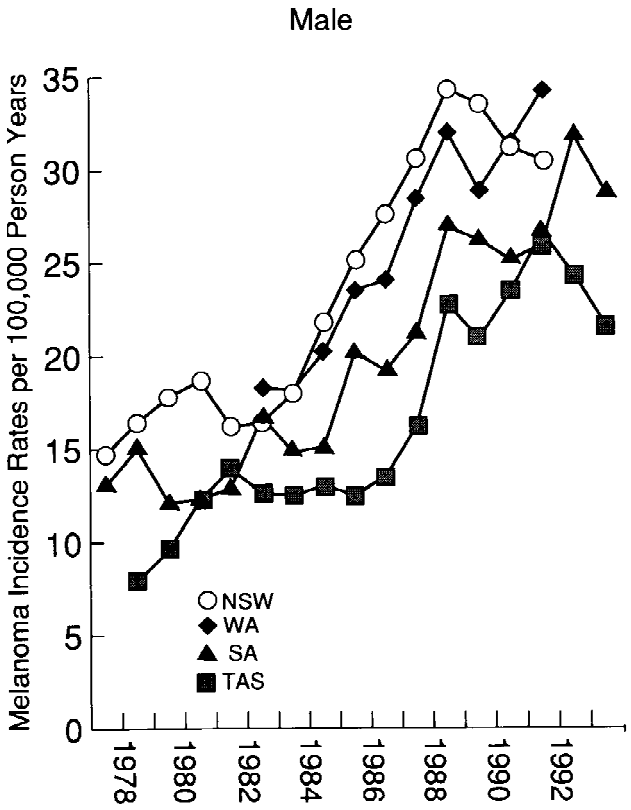


Fig. 2. Age-standardized incidence of melanoma in residents of four states of Australia, 1976–1993: New South Wales (NSW), Western Australia (WA), South Australia (SA), and Tasmania (TAS).

There is plenty of evidence to suggest that advancement of the time of diagnosis is a plausible explanation for the sharp rise in the incidence of melanoma in the 1980s [3]. In the period 1985–1988 the number of Australians having a skin lesion excised increased each year from 2% of the population in 1985 to 3.5% of the population in 1988 [3]. The rise in incidence rates shown in Figures 1 and 2 is exactly what one would expect from advancement of the time of diagnosis consequent upon this activity. However, these rises should have been followed by a fall that should either have returned the incidence to the pre-rise values if screening for melanoma was sustained and produced a continuous gain in lead time, or the incidence rate should have fallen well below the pre-rise levels if it did not. Figures 1 and 2 show that this did not occur and that incidence rates have remained at the new higher levels.

This epidemiological analysis is illustrated further by Figure 3, which extends our published analysis of the Hunter area melanoma epidemic [5]. The Hunter area has a population of over 90% Anglo-Celtic persons and has remained stable at approximately 500,000 for the last 15 years. Figure 3a shows that the number of new cases of invasive melanoma was on a plateau of around 150 a year for the 5 years 1982–1986 (total 736), when it suddenly doubled to 292 new cases in 1988, so that in the 5 year period 1987–1991, 1,294 new cases were diagnosed. If advancement of the time of diagnosis consequent upon increased publicity like ''Goodbye Sunshine'' explains this increase, then the new cases in excess of the 1982–1986 plateau (1,294 − 736 = 558) must have been advanced, that is have come from the years subsequent to 1991. This should have depleted the next 5 years of something like 558 new cases (Fig. 3a). As Figure 3b shows, this has not been observed and, in fact, more new cases were diagnosed in that subsequent 5 year period (1,327 vs. 1,294).

If advancement of the time of diagnosis cannot explain these incidence trends, then what can? A possible and, we would propose, plausible explanation is that the real incidence of histologically diagnosable invasive melanoma in Hunter area men has been at the 1990 levels since the 1970s, but that only some of this disease had the capacity to progress to fatal melanoma. The increased publicity in the 1980s, with the consequent increase of the number of Australians having a skin lesion excised every year, has brought to light this hitherto largely undiagnosed comparatively benign form of the disease. Hence, the rise in incidence has occurred without a rise in mortality.

In summary, this epidemiological analysis of incidence trends suggests that a comparatively innocuous

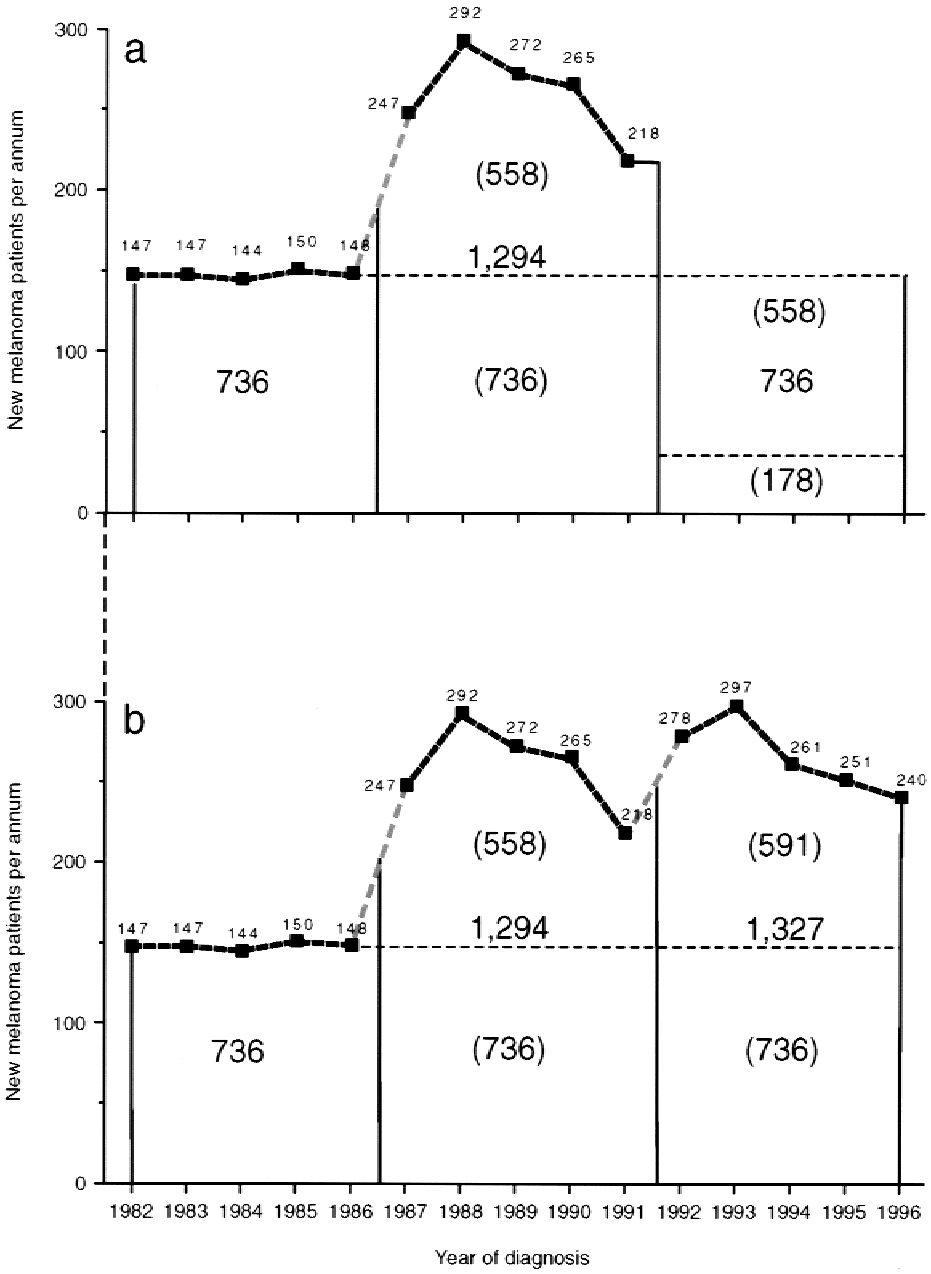


Fig. 3. Number of new patients per annum diagnosed with invasive melanoma in the Hunter area Health Service of New South Wales, Australia. **a:** 1982–1991. **b:** 1982–1996.

form of melanoma, which may have always been with us, has now come to light through widespread informal programs of screening for melanoma that exist in Australia. We would expect that this would also apply in other countries where the incidence of the disease has risen sharply. It may be presumed that this lesion corresponds to the invasive radial growth phase of melanoma, originally described by Clark et al. in 1975 [7], which has been characterized as ''common, incapable of metastasis and indolent'' [8]. It may be that these lesions as a whole have a very low probability of acquiring the additional genetic changes that would cause them to enter the vertical growth phase that leads to metastasis [9], or that some of these lesions lack the capacity to acquire that change. In this regard these forms of melanoma would be akin to the commonest ultraviolet light induced skin cancer, basal cell carcinoma. Such forms of cancer may make up a variable proportion of all cancers. This appears to be true of carcinoma of the prostate and may apply to breast cancer, given the persisting increases in incidence following the introduction of population screening by mammography [10].

## REFERENCES


1. Halsted WS: The training of the surgeon. In: ''Surgical Papers by William Halsted,'' Vol. 2. Baltimore: John Hopkins Press, 1924.
2. Armstrong BK, Kricker A: Cutaneous melanoma. Cancer Surv 1994;19:219–240.
3. Burton RC, Armstrong BK: Recent incidence trends imply a non-metastasizing form of invasive melanoma. Melanoma Res 1994; 4:107–113.
4. Giles GG, Armstrong BK, Burton RC, et al.: Has mortality from melanoma stopped rising in Australia? Analysis of trends between 1931 and 1994. BMJ 1996;312:1121–1125.
5. Burton RC, Coates MS, Hersey P, et al.: Analysis of a melanoma epidemic. Int J Cancer 1993;55:765–770.
6. McCarthy WH, Shaw HM: Trends in the epidemiology, diagnosis and management of melanoma. Cancer Forum 1990;14:6–10.
7. Clark WH, Ainsworth AM, Bernadino EA, et al.: The developmental biology of primary human malignant melanomas. Semin Oncol 1975;2:83–105.
8. Guerry D, Synnestvedt, Elder AE, Schultz D: Lessons from tumor progression: The invasive radial growth phase of melanoma is common, incapable of metastasis, and indolent. J Invest Dermatol 1993;100:3425–3455.
9. Clark WH Jr, Elder DE, Gerry D, et al.: Model predicting survival in stage 1 melanoma based on tumor progression. J Natl Cancer Inst 1989;81:1893–1904.
10. Feuer EJ, Wun LP: How much of the recent rise in breast cancer incidence can be explained by increases in mammographic utilization? Am J Epidemiol 1992;135:1423–1436.